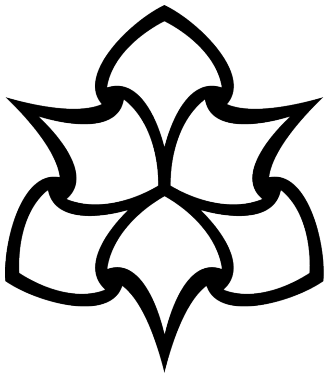

Chapter 7

Memory and Amnesia

(contributed by Andrew Parker)

Introduction

Memory has been investigated extensively by those involved in neuropsychological research. This research has taken many forms encompassing practically all types of memory ranging from that which is processed for the briefest of periods of time to memory across the lifespan. This chapter assesses the contribution that neuropsychologists have made both through the study of those individuals with brain damage and by use of neuroimaging procedures with healthy volunteers. Memory itself, at a most general level, refers to our ability to acquire, retain and retrieve information. This information is stored in the brain, and thus analysis of those who have sustained damage to the brain or techniques that allow us to image brain activity provide us with means by which we can understand memory.

The fact that memories are stored somewhere in the brain, *and* that they consist of activities involved in acquiring, storing and retrieving this information points to two general theoretical approaches that have provided guiding frameworks in the study of memory. The first approach has often been labelled the systems approach and takes the view that different types of memory are located within different regions of the brain (e.g., Cohen and Squire, 1980; Schacter and Tulving, 1994). The second approach has been called the process approach and takes the view that memory is composed of different processes that may recruit similar or different neural regions depending on the task facing the individual (e.g., Cermak, 1994; Roediger, Weldon and Challis, 1989; Verfaellie, and Keane, 2002). Of course this dichotomy simplifies many aspects of past and ongoing research; memory is likely to consist of multiple neural regions and multiple processes (Parkin, 1999). In light of this, the current chapter emphasises the idea that memory consists of both systems and processes and that both views are important for a comprehensive understanding of this topic.

We start by considering short-term and working memory before moving onto long term memory. This outline appears to emphasise the memory systems approach, and indeed in some ways it does. However, this is purely for the sake of exposition, as the reader will soon become aware of how these ‘so called’ systems operate, and thus of the processing activities performed by these systems.

Short-term memory and working memory

The idea of short term memory (STM) has a long history but its most influential form was developed by Atkinson and Shiffrin (1968) and can be seen in figure 7.1. Their “modal model” of memory distinguishes between a sensory memory store (which stores sensory impressions for very brief periods of time), a short-term memory store (which can hold information over longer periods through mental rehearsal) and a long-term memory store (into which information is passed following processing by the short-term store). The model proposes that the memory stores (systems) are essentially unitary; that is indivisible into separate sub-components. However this notion has been subject to revision following empirical investigations into both short-term and long-term memory.

With respect to short-term storage the concept of a unitary STM system presented a number of problems and has undergone subsequent revisions. These revisions eventually led to an alternative conception in which STM is composed of a number of sub-systems. This multi-component model, referred to as working memory, is most closely associated with the work of Alan Baddeley and colleagues (e.g., Baddeley, 1986; Baddeley and Hitch, 1974). The structure of working memory is illustrated in figure 7.2**.** It consists of a central executive whose function is to direct and regulate the flow of information, and allocate attention and processing operations within the two “slave” systems**;** so called because they are essentially controlled by the central executive. These slave systems are the visuo-spatial sketchpad (which serves the function of integrating

and processing spatial and visual information over short periods) and the phonological loop (which serves the function of storing and processing verbal auditory information over short periods). Although the model was initially proposed on the basis of research with individuals without brain damage, the study of both neuropsychological patients and the use of neuroimaging with healthy controls has been useful in its subsequent testing and development.

Neuropsychological evidence for components of working memory

The visuo-spatial sketchpad is the sub-system responsible for the temporary storage and manipulation of visual and spatial information. One particular neuropsychological test used to assess visuo-spatial memory is the Corsi block test (see chapter 2). In this task nine identical blocks are arranged in front of the participant in such a manner that there is no apparent order or pattern to their placement. Following this, the experimenter taps the blocks in a particular sequence (e.g., touches block 3 followed by 5, 2, 8 etc). The participant is then required to immediately reproduce this sequence. This measures visuo-spatial working memory as the participant has to retain the spatial sequence in order to achieve accurate reproduction. DeRenzi, et al., (1977) found that patients with damage to the right posterior parietal region were significantly impaired on this task. However, the parietal regions do not act by themselves in terms of processing spatial information, the right frontal cortex is also important. For example Pigott and Milner (1994) tested performance on a task that required short-term memory for chequerboard like patterns. In this, participants were presented with a random array of black and white squares. After a short delay the participant was shown the same pattern with one of the boxes missing. It was found that those with right frontal damage were impaired at remembering the spatial position of the missing square. Neuroimaging work also suggests a role for frontal regions in visuo-spatial working memory. For example Smith, Jonides and Koeppe (1996) presented to subjects arrays of dots on a computer screen for 200msec. Following a three second delay, a circle appeared either in the

same or in a different location to one of the dots. Participants were asked to decide if the circle would have covered one of the dots if it had been present at the same time. It was found that this task led to activation in the right frontal lobe. The label 'visuo-spatial' suggests a combination of both visual and spatial processing. In everyday life most visual perceptions contain both visual and spatial information, which may in turn suggest that such features are processed together in the brain. However, it is now becoming clear that the visual and spatial components of working memory can be dissociated. For example, Owen, et al., (1995) reported that damage to the anterior temporal lobes impairs visual working memory whilst leaving spatial working memory intact. Conversely, Levine, et al., (1985) reported that damage to the parietal lobes selectively impairs spatial memory tasks. This double dissociation provides strong evidence that the visuo-spatial sketchpad needs to be sub-divided into separate visual and spatial components, and testifies to the importance of neuropsychological research in advancing our understanding of this component of working memory.

Neuroimaging with healthy controls has also revealed that separate regions are implicated in the processing of visual and spatial information, with visual working memory associated with activations in inferior occipito-temporal regions and spatial working memory associated with activations in parietal regions (Courtney, et al., 1996; Postle, et al., 2003).

In Baddeley's model the phonological loop is actually comprised of a passive storage system called the phonological store and active rehearsal mechanism called the articulatory control process. The former is responsible for the temporary storage of speech based sounds which decay rapidly unless refreshed by the articulatory control process. An everyday example of the phonological loop would be holding a phone number in ones memory just long enough for a call to be made; the number is held in the passive store in speech based form and refreshed by subvocal rehearsal. Studies of brain damaged individuals support the idea that the phonological loop consists of two components. For example it is

possible to observe patients with damage to the phonological store without damage to the articulatory control process (e.g., Caterina and Cappa, 2003; Vallar and Baddeley, 1984). Neuroimaging work also provides broad support for the model as different activations are associated with the phonological store, in BA 40 on the left, and the rehearsal process, in BA 44/45 also on the left (Awh, et al., 1996). However, the location of these sub-systems is far from being resolved. For example Chein, et al., (2003) argued that the putative location of the phonological store around BA 40 may not be an accurate reflection of the functions of this region as it is often activated by non-verbal stimuli, which is inconsistent with its role in phonological processing.

Recent work in neuroimaging has revealed some interesting findings about auditory non-verbal working memory that are not encompassed by Baddeley's model. Arnot et al (2005) found support for the idea that the neural processes that support working memory for the identity of a sound differ from those that support working memory for localising a sound. In their experiment, participants were presented with a two sounds in succession and performed one of two tasks. In one task, participants were asked if the second sound was the same as the first. In the other task, participants were asked if the second sound was in the same spatial location as the first. They found that working memory for the identity of the sound activated a region in the left superior temporal gyrus. In contrast, working memory for spatial location activated parietal cortex posterior temporal lobe and the superior frontal sulcus. Thus the processing associated with auditory non-verbal working memory appears to be functionally segregated with different processing requirements being performed by different neural regions or pathways. In some sense this finding is similar to the results obtained for visuo-spatial working memory in which the neural regions associated with the processing of object identity are different from those associated with object location (see also chp 8, p XXX dorsal vs. ventral streams)

The central executive is considered to be responsible for the attentional control of the other working memory sub-systems as outlined above. It is thought to be primarily dependent upon the frontal lobes such that damage to this region impairs performance on experimental tasks that depend upon executive control and processing (Stuss and Knight, 2002). Research has revealed that the executive may actually comprise of a number sub-processes, each associated with a different neural region (Baddeley, 2002; Shallice, 2002, 2004). More details on the frontal lobes and executive functioning can be found in chapter 11.

Box 7.1 New Additions to Working Memory: The Episodic Buffer

Although the working memory model has stood the test of time and received considerable support, a number of changes and adaptations have been made that further refine the original ideas about short term storage and processing. One important change has been the addition of a new component called the episodic buffer (Baddeley and Wilson, 2002). This component was added for two main reasons. Firstly, because of the need for WM to have some means of integrating visual and verbal codes (which remember are processed by separate sub-systems). And secondly, because of the need for the temporary storage of information that exceeded the capacity of the two slave sub-systems. The latter came to light from the finding that immediate memory span for prose passages is much greater than that for unrelated lists of words. Originally, this fact was attributed to long-term memory. However, Baddeley and Wilson (2002) reported a group of amnesic individuals who despite impaired long-term memory displayed normal levels of prose recall if asked to recall the passages immediately without any form of interference or delay. If the superiority of prose recall is dependent upon long-term memory, then the amnesic individuals should clearly be deficient when tested on this task. Baddeley and Wilson (2002) claim the reason for unimpaired recall of prose is due to the operation of the episodic buffer, which is able to hold and integrate relatively large amounts of information over short periods and act as an intermediary between the two slave systems and long-term memory. This conception of the episodic buffer is not without

criticism, Gooding, Isaac and Mayes (2005), point out that as a theoretical construct it is as yet somewhat underspecified and difficult to test. Also, there is currently no means of assessing the independent contributions of the episodic buffer and long-term memory to prose recall. As a consequence the validity of the episodic buffer awaits the test of time and future research.

Interim Comment:

On the whole, neuropsychological research has provided good support for the idea that working memory comprises a number of sub-components with each involved in the processing or storage of different forms of information. What is becoming increasing clear is that these sub-components are widely distributed across diverse neural regions. A challenge for future research is to answer the question of how these sub-components interact in order to perform the everyday tasks upon which working memory is so crucially important.

Long term memory

General background

Amnesia refers to a particular cognitive deficit in which long term memory is selectively impaired (Victor, Adams and Collins, 1971). There are two broad classes or subtypes of global memory impairments referred to as anterograde and retrograde amnesia (This is illustrated in figure 7.3). Anterograde amnesia is essentially a memory deficit for the acquisition of new information or new learning since the time of the brain damage. Thus those with anterograde amnesia will have problems in remembering things such as what they did the previous day or even a few moments ago. It can be considered a deficit in the ability to update memory, and in many respects those with this form of amnesia effectively live in the past as no (or very few) new memories are laid down. This type of amnesia is

typically associated with damage to the medial temporal lobes (MTLs) and associated structures; namely the hippocampus, the dentate gyrus, the entorhinal cortex, the perirhinal cortex and the parahippocampal cortex (Zola_Morgan and Squire, 1993). Some of these structures are connected to other neural regions important for memory such as the thalamus, mamillary bodies and the prefrontal cortex (see figure 7.4). Retrograde amnesia refers to an impairment in remembering information from the time prior to the onset of the damage**.** In terms of neuropsychological research, these two types of amnesia are often investigated separately with theoretical emphasis and empirical studies designed to assess or characterise the nature of one or the other form. In this chapter we will deal with each in turn and attempt to consider how research with brain damaged individuals and neuroimaging work has advanced what we know about the neural basis of long term memory.

Box 7.2: Causes of Amnesia

A brief overview of some of the causes of amnesia is provided below. However the list is not exhaustive and memory loss is also known to be associated with ECT, dementia and epileptic seizures to name just a few. In spite of this, the causes outlined below are important as these have been the most informative in the neuropsychological investigation of memory.

The Korsakoff Syndrome

Amnesia can actually result from nutritional deficiency that is often associated with chronic alcoholism. Alcohol interferes with the gastrointestinal transport of the vitamin thiamine. Thiamine itself plays an important role in cerebral metabolism and thus a reduction in the amount of thiamine reaching the brain has serious consequences for healthy neural functioning. The memory disorder resulting from thiamine depletion is called the Korsakoff syndrome or sometimes the Wernicke-Korsakoff syndrome (after the two researchers, Carl Wernicke and Sergei Korsakoff, who were initially involved in studying this disorder). The precise neuropathology associated with this syndrome is still the object of investigation but research has implicated the neural structures within the diencephalon (including the mamillary bodies and the thalamus) and even the frontal lobes (Colchester, et al., 2001).

Hypoxia

Hypoxia refers to an inadequate supply of oxygen to the tissues (including neural tissue). Hypoxia can result from heart disorders, carbon monoxide poisoning, arterial disorders, respiratory arrests or even suicide attempts. The neuropathology associated with hypoxia is variable and often widespread (Caine and Watson, 2000) but in terms of memory disorders the hippocampus, thalamus and fornix are often implicated (Aggleton and Saunders, 1997; Kesler, et al., 2001; Reed, et al., 1999).

Vascular disorders

The brain needs a constant supply of blood and this is carried to the brain by a dedicated vascular system. This vascular system consist of a number of major arteries that branch outwards throughout the brain into smaller and smaller arteries that eventually merge with veins which carry the blood back to the heart. Interruptions to the supply of blood can occur for a number of reasons such as by a blockage from a blood clot or *embolism* or from damage to the walls of the artery. In both these cases, the cessation of the supply of blood leads to the brain being deprived of oxygen and nutrients and brings about cell death. Depending upon which arteries are damaged or blocked, different neural regions or structures can be affected. With respect to memory disorders, the important arteries are those that supply the hippocampus, thalamus, mamillary bodies and basal forebrain (von Cramon et al., 1985; O'Conner and Verfaellie, 2002).

Viral infections

Infection with the herpes simplex virus can bring about memory disorders as a consequence of herpes simplex encephalitis. Neuropathological features of this disease include widespread bilateral temporal lobe damage (Colchester, et al., 2001). As structures important for memory reside in the temporal lobe regions (more specifically the medial temporal lobes) then it is not surprising that herpes simplex encephalitis can bring about severe memory impairments.

Head injuries

As the name suggests this form of injury results from a blow to the head in one form or another. The injury can be either penetrating (e.g., gun shot would) or closed. In the case of closed head injury, diffuse damage across widespread neural regions can occur as a result of compression of the brain, the shearing of axons and haemorrhaging. Closed head injuries can often bring about post-traumatic amnesia which can last from minutes, following very mild injury, to months following more severe injury.

Anterograde amnesia and non-declarative memory

Perhaps the most famous case of anterograde amnesia is that of patient HM. This patient was unfortunate to suffer from severe epilepsy and efforts to treat this conventionally (with medications) were unsuccessful. The decision was made to remove the focus of his seizures and this entailed the surgical removal of much of the medial temporal lobe regions in both hemispheres. The operation took place in the early 1950s and left HM with a very severe form of anterograde amnesia. As a consequence of being unable to update his memory, HM was mentally "stuck" in the 1950s (Corkin, 1984). Thus he failed to recognise people he had recently encountered even when these individuals had been in frequent contact with him. He also reread magazines and newspapers because he failed to recognise the fact that he had read them before. On several occasions he made his way back to a previous address following a move to a new house (Milner, 1966; Scovile and Milner, 1957) because he was unable to update his memory for his new address.

In spite of this impairment, his IQ was above normal, as were his language and perceptual abilities (Scovile and Milner, 1957). Furthermore, if asked to keep a string of digits in mind (such as a phone number) he was able to do so very successfully if allowed to make use of mental rehearsal. However if rehearsal was prevented his performance dropped to almost zero (Milner, 1966). HM had some degree of retrograde impairment but this was small in comparison to the severity of his anterograde deficit. For example he was able to recognise the faces of people who became famous *before* but not after his surgery (Marslen-Wilson and Teuber, 1975). However, it has been recently demonstrated the HM has acquired small amounts of new knowledge. For example, O'Kane, Kesinger, and Corkin, (2004) found that he knew a small number of facts about celebrities who had only become famous since his operation. In addition he able to reconstruct an accurate floor plan of the house he moved into since the onset of the amnesia, presumably due to what amounts to thousands of learning trials

(Corkin, 2002). In general, HM shows impaired abilities on recall and recognition memory tasks under conditions that do not allow for extended practice or learning. However he demonstrates intact abilities for perceptual and motor skills learning (Corkin, 2002).

The study of HM raises a number of questions relating to amnesia. Two of these are addressed below and are (i) what are the patterns of intact and impaired performance in amnesia? and, (ii) what precisely is the contribution of the MTLs to memory? Although amnesic individuals such as HM are deficient in acquiring new memories they are not deficient in all aspects of new learning. By examining the patterns of performance across a wide range of experimental tasks amnesia has been a valuable source of information with regard to unravelling the complexity of long term memory systems and processes.

One way to think about this is the distinction made between declarative and non-declarative memory (Squire and Knowlton, 2000) and is illustrated in figure 7.5. Declarative memory (some times called explicit memory) refers to memory for events, episodes and facts. This type of memory is accompanied by conscious awareness that we are using memory in order to perform some task. For example, if asked to recall a list of words, or what you did yesterday, then you are aware that you are using memory in order to recall the information. Non-declarative memory (sometimes called implicit memory) on the other hand is a form of memory that is observed and expressed though performance without any necessary dependence upon awareness. In this case, the individual uses memory without any conscious awareness that memory is guiding or directing their performance. A typical example could be something like riding a bicycle. The ability to ride a bicycle is learned and then expressed through performance (actually riding it without falling off). This behaviour does not demand that the individual recall consciously the actual act of learning. Instead learning is expressed in an automatic fashion. Non-declarative memory comes in many forms and appears to be remarkably preserved in amnesic individuals (Squire

2004). Priming, classical conditioning and implicit learning are three examples of non-declarative memory which are outlined below.

Priming

Priming refers to the influence of a previous study episode upon current performance in terms of accuracy or speed of performance. When psychologists refer to implicit memory, more often than not they mean priming. Priming does not demand awareness of the study episode or the ability of the individual to remember any of the details of the study phase of the experiment. This fact makes it a form of non-declarative memory. An example may help to make this clear. Imagine being presented with a set or words (e.g., CHORD). Later you are presented with a set of word fragments (e.g., C H_ R _) and asked to say what word comes to mind when you read the word fragments. Research has shown that participants are more likely to complete a word fragment with one presented earlier than an equally likely alternative such as CHARM, even though they do not consciously attempt to recall the studied words (Hayman and Tulving, 1989; Roediger, et al., 1992). It is as if the words simply 'pop into mind' in an automatic fashion. This popping into mind of previously studied stimuli is an example of priming. The same phenomenon can be observed in amnesic individuals. For example Tulving, Hayman and MacDonald, (1991) studied priming in patient KC, who had very dense amnesia resulting from damage to the MTLs. KC was presented with a list of words during the study phase of an experiment and then given a test of word fragment completion. They found that in spite of not being able to consciously remember any of the words KC's performance was unimpaired on the word fragment completion task. Essentially, it was as if KC had no deficit at all when memory was tested using an implicit test of memory; KC was just as likely as healthy respondents to complete word fragments with previously studies words. This suggests that whatever memory systems or processes are responsible for these priming effects they are not dependent upon the integrity of the MTLs.

Cognitive research has indicated that the priming effects observed on tests such as word fragment completion are based on perceptual characteristics of the word. Thus if the words are initially *heard* and then tested *visually*, priming is reduced (Rajaram and Roediger, 1993). This perhaps indicates that such priming effects are dependent upon neural regions involved in vision and perception. Sure enough, research with both brain damaged individuals and neuroimaging of healthy controls has led to broad support for this idea. For example, Gabrieli, et al., (1995) found priming effects to be reduced in a patient with damage to the right occipital lobes. Subsequent work has indicated that the left occipital lobe can also support priming (Yonelinas, et al., 2001). With respect to neuroimaging research, priming effects on tasks like word fragment completion are associated with *decreased* activations in regions involved in perceptual processing such as the occipital lobes and the ventral surface of the occipital/temporal region (Koutstaal, et al., 2001; Bäckman, et al., 1997). The fact that decreased activations were found may sound unusual but it is thought to be due to decreased metabolic demands or synaptic strengthening following the initial processing of the word during the study phase (Wagner, Bunge and Badre, 2004).

Intact priming effects in amnesia are not limited to relatively low level perceptual tasks as described above. In addition, performance on memory tasks that require conceptual or meaningful semantic processing is also spared. An example of such a task is word association. In this participants are presented with words such as “belt” or “noisy”. Later, during testing, they are presented with related words such as “strap” or “quiet” and asked to free associate by saying whatever words come to mind. Participants without brain damage are more likely to respond with the meaningfully related words that were presented earlier in the experiment (e.g., strap – belt, quiet – noisy). Levy, Stark and Squire (2004) assessed this form of priming, called conceptual priming, in amnesic patients and

found it to be entirely intact in these respondents too, even when conscious recognition of the presented words was no greater than chance.

Again, this would appear to indicate that priming effects are not dependent upon the medial temporal lobes but instead the contribution of some other neural region which has now been identified by neuroimaging. Wagner, et al., (1997) found that when individuals were required to make conceptual or semantic judgments about words then the left prefrontal cortex became activated. Furthermore, when asked to make the same judgement to the words on a second occasion, a relative decrease in the activation was observed in this same area. This decrease in activation is considered to be the neural signature of priming effects, and parallels that found with perceptual tasks.

Classical Conditioning

Some recent work has focussed on whether another form of non-declarative memory is also intact in amnesic individuals. Classical conditioning is a relatively simple form of associative learning that has been studied in humans using the eyeblink conditioning paradigm and is illustrated in figure 7.6. In its simplest form this involves presenting a conditioned stimulus such as a light or tone just before a puff of air, the unconditioned stimulus, is directed to the eye. The unconditioned stimulus automatically causes an eyeblink response. Following this pairing procedure the light or tone also brings about an eyeblink response (the 'conditioned' response). Gabrieli, et al., (1995) found that amnesic individuals with damage to the MTLs had no difficulty in learning the conditioned eyeblink response in spite of profound declarative memory impairments.

The cerebellum seems to be the critical neural region for this type of non-declarative memory. For example Woodruff-Pak, Papka, and Ivry (1996) found that patients with cerebellar damage were impaired at acquiring the classically conditioned eyeblink response. In Addition, Coffin, et al., (2005) noted that the

cerebellum is particularly susceptible to the toxic effects of prenatal alcohol exposure. In line with this, they found that children with established prenatal alcohol exposure were also impaired at learning a classically conditioned eyeblink response. Neuroimaging research is supportive of the findings with brain damaged patients. Using PET, Schreurs, et al., (1997) found changes in cerebellar activity during the learning and extinction of classically conditioned responses.

Skills and Implicit Learning

Implicit learning is essentially learning without awareness. This form of learning has been assessed by a number of experimental procedures one of which is the serial reaction time task. This may, for example, involve the presentation of a light in one of four horizontal locations. Each location is associated with a response button which respondents are required to press when the light flashes. The lights flash according to a particular sequence or pattern of which the subject is unaware. In spite of being unaware of this sequence, reaction times become faster with practice. This is taken to indicate implicit learning of the sequence. Studies with amnesic individuals indicate that their performance on this task is spared despite profound recognition memory deficits (Reber and Squire, 1994). Another interesting task, developed only recently, is a variation of the radial arm maze initially used in rodent studies of learning. This task involves the presentation of a central circular area on a computer screen. Stemming outwards from this are a number of rectangular arms. A dot is presented in at the end of one of the arms and the respondent is required to move the screen cursor down the arm using a mouse. Once this is done, a dot appears in another arm and s/he is required to trace the cursor back along the first arm and then down the arm which now has a dot within it. Again, unbeknown to the respondent, the dot appears not at random but according to a predetermined sequence. Implicit learning is indicated by decreased reaction times to move around the maze. It has been demonstrated that those with selective damage to the hippocampus

were able to acquire this skill in the absence of knowledge of how the skill was acquired (Hopkins, Waldram and Kesner, 2004).

The above studies demonstrate that whatever neural systems underlie such learning abilities they are not dependent upon MTL structures. Instead learning of this sort appears to be dependent upon the striatum and substantia nigra, which comprise the basal ganglia (see chapter 5 for more details on this structure). Studies of individuals with damage to these structures, such as patients with Huntington's or Parkinson' s disease, display impaired performance on such implicit learning tasks (Knopman and Nissen, 1991; Helmuth, Mayr and Daum, 2000).

The importance of the basal ganglia in implicit learning is backed up by neuroimaging research that demonstrates changes in basal ganglia activity over the course of learning structured compared to random sequences (Thomas, et al., 2004).

Interim Comment

The research outlined above is broadly consistent with the idea that preserved memory functions in amnesia are of the non-declarative type. One of the main characteristics of non-declarative memory is that is a form of non-conscious memory (Squire and Knowlton, 2000). For example most amnesic patients demonstrate priming effects, classical conditioning, and implicit learning without any form of conscious memory for the initial study or learning episode. This may appear to indicate that the primary deficit in amnesia is that of conscious memory with all forms of nonconscious memory intact. However, this may not be the whole story as amnesic patients can sometimes show impairments in certain tasks of nonconscious memory. For example, they show impairments on a number of tasks including priming effects for fragmented pictures (Verfaellie, et al., 1996), more complex forms of classical conditioning (McGlinchey-Berroth, et

al., (1997) and the later stages of skill learning (Knowlton, Squire and Gluck, 1994). As a consequence the characterisation of intact learning abilities in amnesia as being one of non-conscious memory is likely to be too simplistic and no generally agreed conclusions have yet been formed.

Anterograde amnesia and declarative memory

The MTLs have been shown to be important for declarative memory. Damage to these structures brings about an anterograde deficit. Below we consider what neuropsychological investigations can add to our understanding of the distinction made by cognitive psychologists between episodic and semantic memory and how the study of the hippocampus can help to refine the nature of conscious remembering.

Episodic and semantic memory

Declarative memory, as noted earlier, refers to memory for events and facts. Memory for events is often called episodic memory and memory for facts is often called semantic memory (Tulving, 1983). Some researchers claim that the amnesic deficit is one that specifically pertains to episodic memory (Parkin, 1982). This appears to make some sense if we just pause for a moment and consider what this means. You will recall that amnesic patients have no problems with using language or answering general knowledge questions. Both of these depend upon the use of semantic memory. Thus it would seem reasonable to conclude that semantic memory is intact. However, when amnesic individuals are presented with a list of words to recall, or asked about what they did yesterday then their performance is likely to be severely impaired. In both these instances,

the amnesic is being asked to remember a specific event or episode. This, of course, depends upon episodic memory. As amnesic individuals are clearly impaired on tasks of this kind then it would seem reasonable to conclude that episodic memory is impaired. In theoretical terms we could say that amnesia provides support for the distinction between episodic and semantic memory. Unfortunately this conclusion is somewhat premature and we need to consider an alternative explanation. In the above example, the typical amnesic patient could be considered successful at retrieving information that was learned *prior* to the onset of the amnesia (this would be general world knowledge or semantic information learned earlier in their life) but unsuccessful at learning and recalling new information *after* the onset of amnesia. If this is true then the amnesia may simply be a new learning deficit rather than one that can be seen as supporting the episodic–semantic distinction. Support for the episodic – semantic distinction would be more conclusive if amnesic individuals were able to lean new semantic information in the absence of new episodic information. Current findings are somewhat ambiguous on this issue. An early study by Gabrieli, Cohen and Corkin (1988) found patient HM to be severely impaired at learning new semantic facts and thus does not support the episodic – semantic distinction (but see more recent research on HM by O'Kane, Kesinger, and Corkin, 2004). However other research has demonstrated some degree of support. Tulving, Hayman and MacDonald (1991) and Westmacott and Moscovitch (2001) both found new semantic learning could take place in amnesic individuals albeit at a rather slow pace. This conflict may have been resolved by Bayley and Squire (2005) who suggest that new learning of semantic information may take place but only if some of the structures in the MTLs remain undamaged. When destruction is more widespread then new semantic learning is absent.

The role of the hippocampus

The role of the hippocampus has been extensively studied in both animals and humans and is known to be centrally important for declarative memory. However,

declarative memory can take different forms and can be assessed by different means. One form is related to the recognition of a stimulus such as a word, picture or face based upon its overall familiarity. Another is often called recollection and is based upon the retrieval of more detailed information typically in the form of an association between two or more stimuli. Both types of declarative memory are accompanied by conscious awareness but differ in our experience of remembering. This distinction, between *familiarity* and *recollection*, can be easily illustrated. Imagine walking down the street and seeing someone you recognise. Unfortunately you cannot remember their name or any other details about them, this represents *familiarity* based recognition. Later, you recall their name and perhaps where you have seen them before. This is *recollection* based memory. These two components of declarative memory can be measured in a number of ways. One technique involves comparing item recognition memory (e.g., memory for a list of words) with free recall. The idea behind this is that item recognition can be based upon familiarity (if a word on the test list seems familiar then respond 'yes' I saw this word earlier). However free recall requires the retrieval of associations between the stimuli and cannot be based upon familiarity alone. Another technique involves comparing item recognition and associative recognition. For the latter, rather than measuring memory for single stimuli the experimenter presents pairs of words during the study phase (e.g., stay-pool; hall-thin; rage-firm). Later, during the recognition test, some of these pairs are presented again, in the same pairs as before (e.g., stay-pool), whilst others are re-paired (e.g., rage-thin; hall-form). The participant has to try to distinguish between those pairs presented unchanged from those that have been rearranged. As a consequence, associative recognition, by its very nature, requires the retrieval (recollection) of associations.

The distinction between familiarity based memory and recollection has become very important recently as neuropsychologists have attempted to uncover the neural regions responsible each of these. Some argue that the hippocampus is important for all forms of declarative memory, both familiarity and recollection

(Squire and Knowlton, 2000). However, others argue that the hippocampus is important only for recollection (Aggleton and Brown, 1999; 2006). These ideas can be examined in individuals with selective damage to the hippocampus. If the hippocampus is required for both familiarity and recollection them selective damage to this structure should impair both forms of memory. But, if the hippocampus is required for only recollection then it should be possible to observe dissociations between recollection and familiarity. Evidence in favour of the idea that the hippocampus is important for all forms of declarative memory was presented by Reed and Squire (1997). They tested a group of patients with selective bilateral damage to the hippocampal region and found impairments on tests of even single item recognition. More recently, Stark and Squire (2003) compared memory for single items and memory for associations between items in a group of patients with bilateral damage to the hippocampal region and found impairments on both types of test. Thus on the basis of these findings it would appear that the hippocampus *is* needed for *both* familiarity and recollection**,** thus supporting the ideas of Squire and colleagues.

However, these findings have not gone unchallenged. For example, Mayes, et al., (2002) and Holdstock, et al., (2002) studied patient YR who, like the patients mentioned above, had bilateral damage to the hippocampus. YR was assessed across a range of tests designed to tap familiarity and recollection. The researchers found that her memory abilities were impaired when tested with recall type tasks (recollection) but preserved on tests of recognition (familiarity). In addition Holdstock, et al., (2005) tested patient BE, who also has selective bilateral hippocampal damage, and found his associative recognition and recall performance to be more impaired than single item recognition. Accordingly, both YR and BE provide evidence for the theory of Aggleton and Brown (1999; 2006).

Box 7.3: The Diencephalon and Amnesia

Damage to the diencephalon, which comprises the thalamus and hypothalamus (including the mamillary bodies) typically results in memory impairments. In part this is known on the basis of research with Korsakoff amnesia. However, as this

syndrome produces pathology that is more widespread and not limited to the diencephalon, then the precise contribution of this structure remains uncertain. Of course what we need is to assess the memory performance of individuals with more circumscribed lesions. Kishiyama et al. (2005) presented a patient (RG) with bilateral damage to the thalamus following a stroke. Testing revealed impaired recognition memory across a range of materials including words, pictures and faces. Theoretically these results are of importance because they demonstrate that damage to the thalamus can bring about reductions in memory performance. More specifically, as the thalamus receives afferents from the hippocampus these two structures can be thought of as comprising a neural circuit in which damage to either of its components can bring about amnesia (Aggleton and Brown, 1999; 2006). As the thalamus itself comprises a number of distinct nuclei, it has been proposed that different mnemonic processes are subserved by some of these nuclei. For example Aggleton and Brown (1999; 2006) claim that the anterior nuclei are important for recollection whist the medial dorsal nuclei are important for familiarity based recognition. Unfortunately, this has yet to receive support from human studies and some evidence actually runs contrary to its proposal. In particular, Edelstyn et al., (2006) found that damage to the medial dorsal thalamic nuclei did not impair familiarity based recognition.

Interim Comment:

Theories about hippocampal function have been the focus of investigation in the animal modelling literature. Of course it is not possible to ask an animal if they are conscious of a specific event or are able to recollect details of some particular experience. As a consequence, understanding hippocampal functioning in animals has, of necessity, taken a different route. However, elements of both the human and animal research can be seen to map onto one another. For example, largely on the basis of work with rodents, Eichenbuam (2002) has advanced the idea that the hippocampus is important for the acquisition and expression of *relational* memories. An important property of relational memory is that associations are formed between multiple elements of an episode but, in spite of being associated, these elements maintain their own independent identity. Thus an association between A and B is not ‘fused’ together in some ridged and inseparable representation but rather stored in a manner that allows each element to be accessed, compared and processed in relation to other elements. These relational representations can be altered,

added to and changed over time. Thus relational representations formed by the hippocampus are said to be flexible. For example, if A is related to B, and B is related to C, then a flexible representation of these pairings allows one to make an inference about the relationship between A and C even though they have never been paired together.

The research with brain damaged individuals reviewed earlier provides some support for the relational account of hippocampal function, as do some recent neuroimaging studies that find greater hippocampal activation during the formation and remembering of stimulus pairings. In addition, it has been shown that solving problems of the type A-B, B-C, A-C also leads to greater activity in the hippocampus (Heckers, et al. 2004).

So, where do all these findings leave the debate regarding the functions of the hippocampus? Unfortunately, as yet the picture is still unclear and only further research is likely to clarify it. In terms of research on amnesia this will be an interesting debate to keep an eye on as it will help to sharpen our understanding of the precise functions of the hippocampus and the contribution it makes to declarative memory.

Memory processes

So far this chapter has dealt with research that provides broad support for the idea of memory systems. The notion that memory systems differ with regard to how they process information has been implicit in much of the foregoing and research with brain damaged individuals has highlighted the importance of component process involved in different types of memory task. In this section we deal with the concept of memory processes in a more explicit manner and consider how such ideas from mainstream cognitive psychology have been integrated and advanced by neuroscientific work. One of the most significant achievements of the cognitive approach to learning and memory relates to the

development of theories and ideas about encoding and retrieval processes and how these interact to influence memory performance. Neuroscientific work has been able to aid the development of cognitive psychology by actually imaging the neural processes that provide the basis for memory formation and remembering. In other words, it is now possible to “see” the hypothetical processes postulated by cognition researchers.

Encoding

Encoding refers to those cognitive activities or processes that are responsible for creating a representation of the event or episode to be remembered. Early work in cognitive psychology demonstrated that the manner in which a stimulus is encoded has direct implications for whether that stimulus will be remembered. For example, Craik and Lockhart (1972) found that performing ‘deep’ meaningful processing on a set of words (e.g., is “cat” a mammal) enhanced memory for those words compared to a condition where shallow processing was performed (e.g., is the word “cat” printed in upper or lower case letters). Craik and Lockhart claimed that memory was nothing more than the remnants of prior processing activity and that deeper processing led to more durable and robust memory traces. Unfortunately for Craik and Lockhart, they were not able to see the encoding activities performed by the brain. Now of course this is a possibility. A number of neuroimaging studies have now been performed in which participants perform either a deep or shallow processing task on a set of stimuli (e.g., words) whilst in the scanner. Collectively the results indicate a number of areas are active in the deep processing condition compared to the shallow processing condition. These include the hippocampus and adjacent MTL regions and the left prefrontal cortex (see Cabeza and Nyberg, 2000 for a review). Some studies have found hemispheric differences such that greater left (vs. right) activations are typical when the stimuli are words (vs. patterns) (Wagner, et al., 1998). Thus different encoding processes that are known to influence memory appear to be associated with different neural regions.

As it is possible to view neural activity associated with encoding, and it is known that certain forms of encoding (deep processing) lead to enhanced memory, maybe neuroimaging can allow us to predict which stimuli are most likely to be remembered on the basis of how much activity is elicited during encoding. This is indeed the case. For example Fletcher et al (2003) required participants to perform a deep or shallow processing task on a set of words whilst being scanned. Later, the participants were asked to recall as many of the words as possible. The researchers found a number of things: Firstly, deep encoding led to greater activations in left medial temporal lobes and the left lateral prefrontal cortex; secondly, the amount of activation in these areas actually predicted which words would be recalled; the greater the amount of activation, the more likely the word would be recalled.

Some more recent work indicates that successful memory encoding is related to the *interaction* between the hippocampus and other cortical regions to which it connects; greater interactions lead to greater probability of recall success (Ranganath et al, 2005). Other research has shown that not only can we predict which words will be recalled by monitoring neural activity during the encoding of the word, but the neural activations that occur milliseconds *before* a word is encoded can also predict memory success (Otten et al, 2006).

So far only half the story has been told. Memory is as much about retrieval as it is about encoding (Tulving, 1983). What has neuroimaging research told us about the act of retrieving information from memory?

Retrieval

Retrieval refers to accessing information stored in memory. In cognitive research, retrieval can be broken down into a number of subcomponents called retrieval mode, ecphory and recollection (Tulving, 1983). For further details see focus box.

Box 7.4: Components of Memory Retrieval

Retrieval mode refers to a form of “mental set” in which the individual directs attention to the act of remembering and makes use of cues in order to recall information. For example, suppose someone asks me if Zechariah was at the fancy dress party I went to last week. The name “Zechariah” the event “party” and the time “last week” all act as potential retrieval cues. In attempting to answer the question I will put them all together and prepare to probe my memory of the event. Ecphory, is the term used to refer to the interaction between the retrieval cue and the stored memory trace. For example, the stored memory trace of who was at the party will interact with the retrieval cues “Zechariah” “party” etc and allow me to recover the stored information of who was at the party. Recollection is when the individual becomes aware of the information retrieved. In this case I become aware that Zechariah was indeed at the party as I recall him swinging from the chandelier in an astronaut suit. As with encoding, these processes are unobservable but neuroimaging procedures may again allow us to “see” some of these activities and help to establish a neural basis for retrieval.

Retrieval mode was examined by Lepage et al (2000). They found a number of regions to be activated, including the right prefrontal cortex (and to a much lesser extent the left prefrontal region), during retrieval. This was found irrespective of whether or not retrieval was successful, and was taken to indicate the neurocognitive processes underlying the establishment and maintenance of the ‘mental set’ in which attention is directed to the act of remembering. The involvement of the right prefrontal region has taken-on added significance given the fact that numerous studies appear to show similar activations during episodic memory retrieval (see below).

Distinguishing between ecphory and recollection is difficult and research has tended to compare whether different areas of the brain are activated when retrieval is successful (in which case *both* ecphory and recollection have presumably taken place) to conditions in which the retrieval is unsuccessful (in which case ecphory and recollection have not taken place). For example Stark and Squire (2000) compared which regions of the brain were active when participants recognised words (or pictures) presented earlier during the experiment compared to words (or pictures) that were not presented earlier. The

assumption is of course that stimuli presented earlier will lead to ecphory and recollection whilst the new stimuli would not lead to such processes. They found significant activation in the left hippocampus during word recognition and bilateral activation of the hippocampus during picture recognition. However, a potential problem with this study is that participants may not have recognised some of the words and pictures presented earlier. What is needed if we really want to image ecphory and recollection is to compare activations that occur when participants actually recognise the stimuli to activations in which participants fail to recognise them. This requires the use of event related fMRI (see chapter 2). Using this method Dobbins et al (2003) who found correct recognition responses were associated with enhanced activations in the left hippocampus and the parietal cortex. The finding of enhanced neural responses in the hippocampus is to be expected on the basis of work with brain damaged individuals. However the significance of the parietal activations is somewhat unclear even though it has been observe in a number of experiments (McDermott and Buckner, 2002; Rugg, 2004).

Encoding and retrieval interactions

On the basis of the previous discussion you may be forgiven for thinking that encoding and retrieval are two entirely separate processes. However, cognitive research has come to place emphasis on how these two processes interact with each other in order to enhance memory. The manner in which encoding and retrieval processes interact has been the focus of much research and forms the foundation of a particular framework called Transfer Appropriate Processing or TAP for short. TAP has its roots in memory research dating back to the 1970s but has been more formally specified by Roediger and colleagues (e.g., Roediger, Weldon and Challis, 1989). Basically, TAP states that the most important factor determining successful memory is the extent to which encoding and retrieval processes overlap. If retrieval processes overlap or recapitulate the same mental processes that occurred during encoding then memory will be

successful. An example may help to make this clear. Morris, Bransford and Franks (1977) presented participants with words such as EAGLE and asked them to perform one of two tasks on these words; a semantic-meaningful task (e.g., is an eagle a large bird?) or a rhyming task (e.g., does eagle rhyme with legal?). Later, participants were given one of two tests of memory. One thought to rely on meaning (a recognition test) and one thought to rely on the sounds of the words (deciding if the test words sounded similar to the studied words). It was found that performance on the test that depended upon meaning was enhanced by the earlier meaning based encoding task, whilst performance on the sound test was enhanced by earlier rhyme based encoding task.

Presumably, the reason why encoding – retrieval overlap is important is that retrieval reflects the recovery or reactivation of the memory trace laid down during encoding. Morris et al. were not able to observe such processes in the brain but yet again neuroimaging research allows us to observe these processes and see if their overlap is as important as the TAP framework suggests. Vaidya et al, (2002) made use of fMRI in order to examine if the cognitive/neural processes used to encode pictures of objects into memory were also active when retrieving this information. Participants were scanned whilst encoding words and pictures into memory and also later whilst retrieving this information. The researchers found that during the encoding of pictures a number of neural regions became activated including the fusiform gyrus and inferior temporal gyrus bilaterally, and the left mid-occipital gyrus. During retrieval a subset of these regions became active once again, most notable in the left hemisphere. These regions are known to play a role in aspects of object recognition and Vaidya et al. speculated that during retrieval these regions became reactivated as information about an object's shape and its meaning are being processed.

Interim Comment

Research with neuroimaging has revealed that encoding and retrieval processes may be implemented in different hemispheres of the brain. The so called HERA (Hemispheric Encoding and Retrieval Asymmetry) model was originally proposed by Tulving, et al., (1994) and Nyberg, Cabeza and Tulving (1996) and was meant to summarise a number of findings that indicated that the left prefrontal regions showed greater activations during encoding while the right prefrontal region showed greater activation during retrieval. Although subject to some criticisms (Lee et al., 2000) these findings have been shown to be remarkably robust (Habib, Nyberg and Tulving, 2003). It would seem that although encoding and retrieval processes do activate similar neural regions, as predicted by TAP, they also possess differences. Some of these differences are related to the manner in which processing activity is lateralised.

Retrograde amnesia and autobiographical memory

As mentioned earlier retrograde amnesia refers to an impairment in remembering information from the time prior to the onset of the disorder or injury to the brain. Although it often co-occurs with anterograde amnesia (Kapur, 1999) it can also occur in relative isolation and is called focal retrograde amnesia (e.g., Kapur et al, 1989). Most often, impairments are greatest for more *recent* events leading up to the injury or disease (Squire, 1992). This produces a situation in which memory for more distant events, such as those in childhood, is actually better than memory for more recent events. This is the reverse of what is found in those without retrograde amnesia who display superior memory for more recent events. The temporal extent of the retrograde impairment can vary quite widely. For some individuals the impairment may be for the previous few months or years. For very severe cases, the extent of impairment can be across the whole life span (Cermak and O'Connor, 1983).

In addition those individuals with retrograde amnesia can often display a range of deficits in recalling pre-morbid memories. These can include: (i) memory for personal episodes and events from their lives such as a birthday party or holiday, (ii) personal semantic information such as who they are, their characteristic traits and preferences, (iii) public and news events, such as who won the general election on some particular date and also famous people and personalities, like politicians and TV stars. Interestingly, on some occasions, deficits can be more severe for certain types of memory. For example Manning (2002) examined patient CH with retrograde amnesia resulting from hypoxia following a cardiac arrest. Testing revealed that CH had relatively preserved new learning abilities (i.e., limited anterograde amnesia), however, memory for autobiographical information was particularly impaired and more so for personal events and episodes.

If you were asked to recall something you did yesterday or maybe from a party a few years ago what sort of information do you recall? Many people report recalling visual images of the event or seeing what happened (Brewer, 1995). It is now thought that visual imagery may play an important role in the retrieval of memory for personal events and experiences (autobiographic memory) and enable us to mentally relive and re-experience our past (Rubin, Schrauf and Greenberg, 2003). If this is true then one would expect that individuals who are deficient with respect to processing visual information may also have impaired access to their autobiographical memories and feel unable to relive those memories in the same way that we can. Recent studies are consistent with this idea. Greenberg et al (2005) studied patient MS with a visual processing deficit (agnosia) who had sustained damage to a number of regions including the temporal and occipital lobes. Not only did MS display a severe retrograde deficit, but the autobiographic memories he did manage to recall were unlike those of control participants in a number of ways. For example, when rating his memories in terms of how real or vivid they felt MS was significantly impaired. His

memories were simply lacking in the types of detail and recollective experience that make our memories of incident and events so compelling.

Why should visual imagery play such an important role in the retrieval of our past? A neuroscientific explanation relates to the way in which memories are stored and retrieved. Memories, especially autobiographical memories, are complex and often involve the interplay of a number of different senses such as vision, audition, olfaction etc (Hodges, 2002). Damasio (1989) advances a theoretical account that claims the processing and storage of such a variety of information takes place not in one neural region but across multiple regions with each involved in processing a different aspect of the original event. For humans at least, the visual sense is particularly important. When it comes to retrieving the autobiographic memory then multiple neural regions become activated and provide the basis of our re-experiencing the event. These interacting regions can be seen as being dependent upon one another and, as a consequence, damage to one region can effectively disrupt the activation process from spreading to other neural regions**.** This may either prevent memory retrieval or at least disrupt the retrieval of some of the details of the experienced event. Damasio's theory has been used on a number of occasions to account for aspects of the retrograde deficit (e.g., Hunkin, 1997) and in relation to patient MS the explanation could be that damage to the regions of brain responsible for visual processing (e.g., occipital lobes) disrupt retrieval processes and either prevent access to the autobiographic memory of the types of details that lead to vivid recollection (Greenberg, et al. 2005). Interestingly, the MTLs would still appear to be important for more vivid and detailed recollection. For example Steinvorth, Levine and Corkin, (2005), found that Patient HM, although able to retrieve distant memories, often substituted gist for specific details. Thus the ability to recall personal experiences and almost 'relive the moment' depends upon the intact functioning of multiple neural regions.

Neuroimaging of autobiographic memory.

The idea that autobiographic memory is dependent upon a diverse set of interacting neural regions has received some support from neuroimaging research. In a review, Maguire (2002) reported that autobiographical retrieval leads to the activation of a network of areas including temporal and parietal regions, the medial frontal cortex, the cerebellum and the hippocampus. However, different experimental studies often reveal different activations. Maguire claims this is likely to be due to a number of factors, such as the variety of means by which autobiographical memories are elicited, the relative recency of the memories, differences in the amount of effort required to recall a memory and the amount of time allowed for each recall and response. All these differences make comparisons and generalisations quite difficult and clearly much research needs to be carried out in this important and interesting area.

As mentioned earlier, patients with retrograde amnesia often display a temporal gradient of memory loss affecting more recent (vs. more distant) memories. How can this characteristic pattern be explained? Some argue that following the encoding of an event, memories undergo a slow consolidation process and that this is dependent upon the hippocampus (Squire, 1992; Teng and Squire, 1999). Thus initially, a newly formed memory is actually quite unstable. Consolidation processes work to make the memory stable and increase its strength and resistance to forgetting. More specifically, it has been proposed that the hippocampus is responsible for retrieving only relatively recent memories. Following the passage of time, and the consolidation process, it becomes possible to retrieve memories independently of the hippocampus. This idea has received support from research with animals and humans. For example, Zola-Morgan and Squire (1990) trained monkeys to discriminate between a set of different objects over a period of weeks. Following lesions to the hippocampus the monkeys were tested on their memory for the previously learned objects. If the hippocampus is required for the retrieval of more recent memories then lesions to this structure should produce a greater impairment for the most

recently acquired objects. This was indeed the case; memory was most impaired for the objects learned a few days ago and was best for those acquired weeks ago. In humans, Bayley, Hopkins and Squire (2003) presented amnesic individuals, whose pathology was limited to the hippocampal region, with the cue word autobiographical memory test. They were asked to recall memories from the first third of their lives prior to the onset of their amnesia. When compared to control participants it was found that the quality and details of the memories retrieved were virtually identical. Thus it would appear that the recall of more distant memories is not dependent upon an intact and fully functioning hippocampus.

This view is not without its dissenters. For example Nadel and Moscovitch (1997) and Moscovitch and Nadel (1998) propose that the hippocampus is required for the retrieval of both recent *and* remote memories. They note that the temporal gradient of memory loss in some retrograde amnesia cases extends back decades, sometimes up to 30 years. They suggest that it is implausible that any form of physiological consolidation process would take this amount of time, extending sometimes over the entire life of the individual. Their alternative hypothesis is that the hippocampus is always involved in the encoding and retrieval of memories. Over time, memories are subject to reactivation with older memories acquiring a greater number of reactivations. The reactivation process leads to multiple memory traces being formed within the hippocampus and surrounding cortex. When damaged, older (vs. more recent) memories are more likely to be recalled because they are more resistant to loss as they possess multiple retrieval routes Some recent neuroimaging work is consistent with the predictions of this theory; Bosshardt, et al., (2005) found that the amount of activity in the hippocampus actually *increased* with increasing delay over a period of 1 month between encoding and retrieval. The consolidation theory of Squire and colleagues would predict a *smaller* amount of activation over extended periods of time because older memories are hypothesised to be less dependent

upon the hippocampus. As a consequence, it is not clear how the findings of Bosshardt et al could be accounted by the consolidation theory.

Box 7.5: Long-term potentiation and consolidation

Although the consolidation theory of Squire and colleagues has met some challenges very few researches would seriously question the idea that for memories to become stable they must undergo some form of consolidation process. Presumably this process takes the form of cellular and molecular changes at the synaptic level. In spite of being beyond the scope of this chapter, the molecular and cellular basis of memory consolidation has been the object of intensive research and is worth mentioning here. One candidate mechanism thought to be responsible for the consolidation of memories is called long-term potentiation (LTP). The process underlying LTP is complex but, at the risk of oversimplifying matters, it refers to the increased magnitude of the response of the postsynaptic neuron following stimulation by the presynaptic neuron (in experimental animals the action of the presynaptic neuron is mimicked by an electrical impulse). This increased response can be shown to last for hours or months (Barnes, 1979) and thus represents the record of previous neuronal activity. The reason for this is due to an increase in protein synthesis in the postsynaptic neuron (Bourne, et al., 2006; Fonseca, Nagerl, & Bonhoeffer, 2006). Effectively, this leads to a modification or strengthening of the synapse (Martin and Morris, 2002). LTP has been shown to occur in the hippocampus and in the cortex (Bear and Kirkwood, 1993; Ivanco and Racine, 2000) and thus provides a molecular basis for plastic changes in these regions. Linking LTP to overt behavioural changes (learning and memory) has been demonstrated by findings that indicate impaired learning following drug induced blockade of LTP (Davis et al., 1992) and that learning can bring about LTP like changes (Mitsuno et al. 1994; Tsvetkov, et al., 2002). As a consequence, LTP represents a potential mechanism for the enduring cellular and molecular changes underlying consolidation processes in learning and memory. Exactly how these cellular and molecular changes are reflected in the types of memory considered in this chapter is as yet unknown and represents a challenge for neuroscientific theorising and research.

Summary

In this chapter we have considered what neuropsychological research has told us about the systems and processes underlying short-term/working memory and

long-term memory. Through the careful analysis of individuals with brain damage and with the use of neuroimaging procedures we have seen that the concept of memory does indeed encompass and support the idea of multiple memory systems and sub-systems with multiple component processes. It is now clear that the human brain possesses the capacity to represent many different forms of information and that different neural regions performing different cognitive processes are responsible for this capacity. With respect to short-term memory broad support has been gathered for the idea that multiple systems and processes are responsible for the maintenance and manipulation of information currently being processed. Neuroscientific research has assisted in the development and refinement of models of short-term and working memory. By the careful analysis of those individuals with brain damage we have seen that the idea of a unitary short-term memory does not stand up to scrutiny and that different regions of the brain are responsible for maintaining and manipulating verbal information and visuo-spatial information. Neuropsychological work has even provided the impetus for revisions of the working memory model and the incorporation of the so called episodic buffer.

With respect to long-term memory the idea of declarative and non-declarative memory has received considerable support. Furthermore, the precise nature of the sub-systems and processes underlying these forms of memory are being worked out in ever finer detail. For example, non-declarative memory comprises a number of sub-systems that dissociate from one another and are located in different neural regions. Declarative memory comprises a number of processes that enable conscious remembering of past events and research suggests that these processes maybe differentially dependent upon different neural systems and pathways. Conscious recollection appears to be crucially dependent upon the hippocampus and vivid memories may require the additional involvement of neural regions involved in perception. However, this does not mean that our understanding of memory is complete; rather, that it is continuing to develop. Further growth will depend in part upon the theoretical frameworks and ideas that

we bring to bear upon the empirical data, and upon the discovery of new findings that may challenge these frameworks and preconceptions.